

REMARKS

In Applicants' Amendment filed April 12, 2004, independent claims 1 and 49 were cancelled without prejudice and without acquiescence to any previous rejections or objections raised against the subject claims. Claims 2 and 50 were amended so as to recite independent claims and incorporate the language of claims 1 and 49, respectively, from which they previously depended. Claims 5-8, 10-11, and 52-54 were amended so as to not depend from now cancelled claims 1 and 49.

On June 21, 2004, the Office mailed a communication stating Applicants' Amendment filed April 12, 2004 was not fully responsive to the prior office action because no comments concerning the Section 102(b) rejection were included.

Applicants submit herewith further amendments to claims 2, 4, and 50 pending in the application, along with the remarks below to address the Section 102(b) rejection in view of the Wiley reference.

It remains Applicants' position that the claims presented in the instant application are not anticipated under Section 102(b) by the Wiley reference. It is respectfully submitted that the Wiley disclosure of a TRAIL protein contained in 50 mM citrate, neutralized in 1M Tris and adjusted to 10% glycerol does not anticipate the claimed formulations. The claims have been further amended to clarify the invention; namely, that Applicants unexpectedly found that Apo-2 ligand trimers are coordinated and stabilized by the presence of zinc. This was not and could not have been appreciated prior to the present invention because it was not known in the art that TNF ligand family members bound divalent metal ions such as zinc or that the biologically active trimer forms of such ligands could be coordinated and stabilized by a divalent metal ion such as zinc. Indeed, those skilled in the art routinely used other means to form and stabilize trimeric forms of TNF ligand family members, such as through the use of leucine zipper molecules. The Wiley reference does not teach, expressly or inherently, employing any particular excipient or formulation which stabilizes Apo-2 ligand trimer formation. The Wiley reference does not describe any particular aspects of monomer, dimer,

or trimer forms of the Apo-2 ligand or how a formulation of Apo-2 ligand can be prepared to optimize stabilized, trimeric forms of the protein.

For these reasons, it is requested that the Section 102(b) rejection be withdrawn.

Respectfully submitted,
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